A STUDY ON PHYSIOLOGICAL EFFECTS OF ANTIHISTAMINIC DRUGS: A CASE STUDY

SYNOPSIS OF THE THESIS

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Antihistaminic groups of drugs have significant effect on learning behavior of humans. It has been well documented, but how antihistaminic drugs block the receptors is not well reported. There is analogy between functioning of nerves in all groups of vertebrates. The study will find out whether the antihistaminic blocker drugs like Diphenhydramine and Cetrizine has any behavior, or physiological effects on Gold fish, *Carrassius Auratus* on learning and feeding.

It has been reported that post trial blockade of the H1 antihistaminic receptor can affect the appetitive learning in Gold fish by improving long term memory consolidation and or by the additive reinforcing effect of Chlorpheniramine on behavior (Richard, Spiler and Carry 1999) and also inhibition of histaminergic system facilitates the functional recovery in gold fish (Coelho and Medhala 2000).Studies have shown that Histamine has an extraordinarily powerful effect on memory processes, but do not necessarily suggest that this substance has a physiological role in memory modulation (Almeida and Izquierdo 1986).

In vertebrate like rat, it was shown that depletion in brain Histamine was associated with prolongation of response latency to learning (Chiaki Kamei et all 1993).Some studies have shown that in fish histaminergic system has inhibitory effect on learning and memory (Medhalla et al 2000). Several lines of evidence suggest that histamine decreases food intake via H(1)-receptors (H1R) at least in the ventromedial hypothalamus or the Para ventricular nucleus.

Recently, mutant mice lacking H1R were generated and the interaction between the histaminergic system and leptin-induced suppression of food intake was evidenced by using these mice (Morimoto and Yamamoto 2001). Morimoto et all (2000) has shown that Histamine release was significantly increased by leptin administration (1.3 mg/kg, i.p.). This finding suggests that leptin activates the histaminergic system in the hypothalamus, which may contribute the expression of leptin-induced anorectic effect

Research studies on learning and memory appear to be a powerful tool for the comparative study of cognition. Knowledge of cognitive capabilities and

their neural basis in fish could contribute to the understanding of the evolution of the brain and behavior in vertebrates. The teleost telencephalon, which was once considered an olfactory system, is now known to be involved in more complex functions (Fernanda R et all 2008**)**

However, research results on the effects of histamine on learning, memory and reinforcement processes have not been conclusive, either because of the lack of specific methodologies for investigating this neural system or histamine is modulating the behavioral components that affect learning and memory (Fernanda R et all 2008**).** Clinical observation that some antidepressants and antipsychotics with antihistaminic activity stimulate food intake and increase body weight, histamine has been thought to be an anorectic agent. (Morimoto et all 2001).

Fish show cognition and adaptive behavior, fish show highly developed spatial navigation abilities, nonassociative learning such as habituation, precise timing abilities, Pavlovian conditioning, operant behavior motivated by aversive stimuli such as shuttle box behavior, negatively reinforced avoidance, and food-reinforced lever pressing positively reinforced responding Few studies have shown that the fish model of development can be used in studies of learning, memory, and cognition (Edward D et all 2009).Therefore fish was used as a model of learning in this research.

To further investigate and shed more light on this matter we have undertaken this research study.

To learn more about the analogy of nerves between vertebrates and to shed light on behavior/Physiological effect of antihistaminic Drugs on Gold Fish we undertook the study on Feeding behavior and learning behavior.

The entire research work has been studied under the following aspects:

I. **The effect of Cetrizine on feeding behaviors of *Carrassisus Auratus***

II. **The effect of Diphenhydramine to be compared with Cetrizine on feeding behaviors of *Carrassisus Auratus***

III. **The effect of Cetrizine on learning behavior of *Carrassisus Auratus*.**

IV. **The effect of Diphenhydramine to be compared with Cetrizine on learning Behavior of *Carrassisus Auratus***

V. **Effect of Cetrizine and Diphenhydramine on Liver of fishes, histological changes observed**

I-The effect of Cetrizine on feeding behaviors of *Carrassisus Auratus*

The study site was Antech Diagnostic labs, and Medgar Ever College, and Fish used was locally available Gold Fish and Drug Cetrizine was available locally Cetrizine, was administered as Intraperitoneal injection in dose of 1mg to 10 mg in graded concentrations with Img for the first fish and 10 mg for the last fish. A total of three trials were done using Cetrizine. When Compared with Control and Saline the fishes treated with Cetrizine had ingested more fish flakes. Similar results were obtained in the revalidation trials, showing that Cetrizine did play a role in feeding behavior of fish.

II- **The effect of Diphenhydramine on feeding behaviors of *Carrassisus Auratus* and data to be compared with Cetrizine**

Diphenhydramine was administered as Intraperitoneal injection in dose of 1mg to 10 mg in graded concentrations with Img for the first fish and 10 mg for the last fish. A total of three trials were done using Diphenhydramine. When Compared with Control and Saline, the fishes treated with Diphendryramine had ingested more fish flakes. Similar results were obtained in the revalidation trials, showing that Dipehnhydramine did play a role in feeding behavior of fish. The result of this study was compared with Cetrizine and when compared with Cetrizine the data in all the trials was similar and having similar results in the feeding behavior suggesting that the Antihistaminergic system increased the feeding behavior in Gold Fishes.

III. **The effect of Cetrizine on learning behavior of *Carrassisus Auratus***

Cetrizine was administered as Intraperitoneal injection in dose of 1mg to 10 mg in graded concentrations with Img for the first fish and 10 mg for the last fish. A total of three trials were done using Cetrizine. When Compared with Control and saline, the fishes treated with Cetrizine took less time in reaching to food sources. Similar results were obtained in the revalidation trials, showing that Cetrizine did play a role in learning behavior as fishes were able to reach to food source faster

IV - The effect of Diphenhydramine on learning Behavior of *Carrassisus Auratus* and data to be compared with Cetrizine

Diphenydramine was administered as Intraperitoneal injection in dose of 1mg to 10 mg in graded concentrations with Img for the first fish and 10 mg for the last fish. A total of three trials were done using Diphenhydramine. When Compared with Control and Saline, the fishes treated with Diphenhydramine took less time in reaching to food sources. Similar results were obtained in the revalidation trials, showing that Diphenhydramine did play a role in learning behavior as fishes were able to reach to food source faster. This was compared with the data from Cetrizine on learning and it was found that the data in all the three trials with drug, saline and control had similar results, proving that Antihistminergic system helped in learning behavior Gold Fish

V -.**Effect of Cetrizine and Diphenhydramine on Liver of fishes, histological changes and on space on preference test .**

Histological changes were studied on the liver of fish after treating the fish with Cetrizine and Diphenhyramine in does of 5, 15,20 mg and fishes dissected after 48 hours and slides observed did not show any (inflammatory,structural,cytoplasmic,necrotic) changes in liver hepatocytes , of the Gold fishes. Slides were made from the middle most part of fish liver and stained with Hemotoxylin and Eosin and observed under light microscope. Space preference test was found inconclusive.

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